



6th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV

25–28 October 2004 - Washington, DC, USA

MITOCHONDRIAL DYSFUNCTION OF HAART-RELATED HYPERLACTATAEMIA IS DEMONSTRABLE BY NON-INVASIVE STUDIES

Antiviral Therapy 2004; 9(6):L24 (abstract no. 35)

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OBJECTIVES: Hyperlactataemia is one of the most serious adverse effects of highly active antiretroviral therapy (HAART). Mitochondrial DNA (mtDNA) depletion and mitochondrial respiratory chain (MRC) dysfunction is demonstrable in liver or skeletal muscle, but they constitute invasive methods with limited clinical use. We describe herein a non-invasive technique to detect mitochondrial dysfunction in HAART-related hyperlactataemia.

METHODS: We have developed the forearm aerobic exercise test (FAET) to measure oxygen saturation in forearm venous blood before, during and after aerobic exercise. Lactate measurements before and after FAET assure absence of anaerobic effort. We have performed FAET in asymptomatic HIV controls and in an HIV-infected patient undergoing HAART-related hyperlactataemia and 6 months after resolution. Simultaneously we measured mtDNA content by quantitative real-time PCR and enzymatic MRC activities by spectrophotometry in biopsied skeletal muscle homogenate.

RESULTS: The symptomatic hyperlactataemic patient has a mtDNA content of 47% with respect to control values (100%), which increased to 110% 6 months after recovery. MRC activities of mtDNA encoded complexes I, III, IV and V were diminished during the acute episode [39%, 61%, 64% and 45%, respectively, compared with controls (100%)] and returned to normal 6 months afterwards. The FAET performed on the hyperlactataemic crisis showed a decrease of 46.44% in the mean venous haemoglobin saturation during aerobic exercise with respect to control values (100%), and this abnormal oxygen usage disappeared 6 months later.

CONCLUSION: Mitochondrial functionality analysis and the FAET match clinical manifestations in an HIV patient undergoing symptomatic HAART-related hyperlactataemia and after clinical recovery. The FAET could be a non-invasive useful tool for the screening of mitochondrial abnormal function and reduced oxygen consumption.

ACKNOWLEDGEMENTS: Study supported by Fundación para la Investigación y la Prevención del SIDA en España (FIPSE 3102/00), Fundació la Marató de TV3 (02/0210), Redes de Investigación en Mitocondrias (V2003- REDC06E-0) y SIDA (Redg 173) and Suports a Grups de Recerca (2001/SGR/00379).

2004-10-25

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